

The Clinical Pathology of the Digestive Tract

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ACUTE abdominal conditions so frequently cause death, and chronic lead to so long continued ill-health and, often, dangerous complications, that it is obvious that diagnosis with a view to treatment should be made as soon as possible. It is essential that the diagnosis be as certain and exact as may be, for, in the acute case, its accuracy may be a matter of paramount importance, while, in the chronic, whether the treatment resulting be medical or surgical, it is likely to entail the patient's being away from his occupation for some weeks; if he be not on the way to recovery at the end of that time it will have been wasted.

In arriving at a diagnosis, the most important help of all is a careful account of history and symptoms. In a certain number of cases, especially in the acute, one can be morally certain of the exact pathological condition from the patient's own story, and a diagnosis which does not fit in with it should be viewed with suspicion.

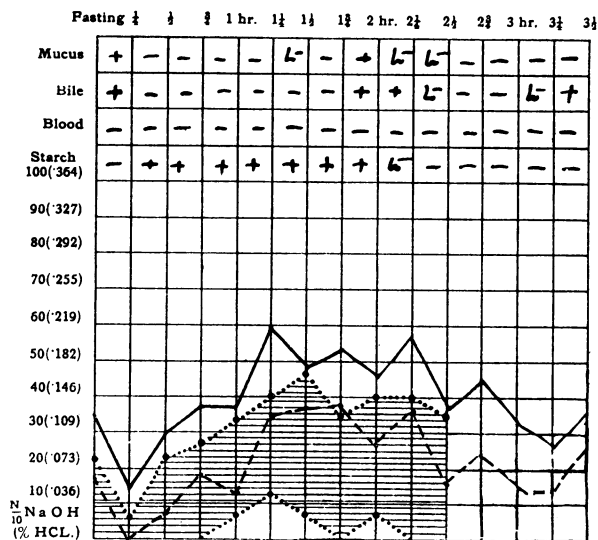
Next comes physical examination. In the acute case this is often sufficient to complete a diagnosis already considered likely, but in the chronic the assistance obtained is frequently not so great. In the latter it is advisable, if at all possible, to examine the patient on two separate occasions—when symptoms are active and again when they are quiescent. When symptoms are active, the site of pain or tenderness will be readily found. It may, however, be diffuse, covering a large area and not referable to any particular organ. If this be so, it is likely to persist and be more defined when a less active phase is present. On the other hand, if the trouble is quiescent and no symptoms are at the time complained of, physical examination may yield very scant result.

When all the information possible has been gained in these ways it should be possible to arrive at a tentative diagnosis. It is then that other methods may be called in either to confirm or negative it, and the gaze turns in the direction of radiology and the laboratory.

Of the investigations carried out by the clinical pathologist in digestive disorders, probably the most generally useful is the fractional test meal.

Fractional Test Meal.—The fractional method of investigating gastric secretion was first described in America by Rehfuess in 1914, but was not practised in this country until six years later, when the technique was introduced by Ryle. At the beginning Ryle and Bennett carried out fractional test meals on one hundred volunteer students suffering from no detectable digestive abnormality, and from the data thus obtained determined what the findings are in normal people. For this piece of work a debt of gratitude is due to them from all who are interested in the study; the limits which they placed for normal curves are generally accepted and form a standard by which aberrations may be judged.

Since then a great many investigations have been carried out by gastro-enterologists and a most voluminous literature has grown up. A certain amount of



1. CURVE FROM NORMAL PATIENT.

Free hydrochloric acid is within normal limits. Combined acid is constantly about 20. Emptying, as is indicated by the disappearance of starch, takes place in two hours. Bile is present intermittently and there is a little mucus.

The shaded area represents the limits for free HCl. (dimethyl indicator), of 80 per cent. of normal people.
 — — — — — represents free HCl. ————— represents total acidity.

discussion has taken place from time to time, and, as might be expected, criticisms of the method have been made, some of which are :—(a) That the tube acts as a foreign body in the stomach. Pavlov and Beaumont proved that foreign bodies in the stomach do not alter its secretory action. (b) That the unappetizing nature of the meal diminishes gastric secretion. Appetite secretion is a very doubtful quantity, and many writers do not believe that it occurs at all. If it does it cannot be denied that the absence of mastication and the insipid nature of the gruel swallowed will diminish it, but this is, probably, rather an advantage, since it will render the results more comparable from one person to another. (c) That emotional disturbance inhibits or increases the gastric secretion during the test. The emotional disturbance is almost negligible, especially if the technique be explained to the patient beforehand and his attention distracted during the test by the reading of something interesting. The proportion of patients who have any real difficulty in swallowing the tube, or who seriously resent it, is small. In fifteen years I have come across only three patients who were unable to swallow the tube or keep it down comfortably for the required length of time. (d) That the secretory response is variable from day to day in the same person. When the conditions and technique of the test are exactly standardized, it has been found that there is a remarkable agreement in the curves obtained when the meal has been repeated on several occasions at intervals of a day or two. The time of emptying is very constant, and the general

conformation and height of the curve vary but little. (e) That the acidity is different at different stomach levels. The tube should always be kept at the same level throughout the test. In any case it would seem unlikely that, in view of the fluid nature of the gruel used and the motor activity of the stomach during digestion, very complete mixing should not take place.

There is no doubt that, whatever the theoretical objections which may be raised, in actual practice the test has proved itself of great help in clinical diagnosis. It must be remembered, however, that it only tells us what is happening during digestion and does not, as a rule, make a diagnosis. No gastric analysis should be labelled with the name of a disease, and the most it can do is to help us, when taken in conjunction with the history, clinical, radiological, and other pertinent examinations, to infer that a certain condition is likely to be present. The exception to this rule is when a gross obstruction is present and when it is generally possible to be quite dogmatic.

Occult Blood.—Another test which should be generally carried out in conjunction with the fractional test meal is the examination of the fæces for occult blood. Everyone is familiar with the black, tarry stools which follow on a large gastric or duodenal hæmorrhage. Something which is not so generally appreciated is that an ulcer, when active, although it may not give rise to as much blood as will produce a change in colour of the stools, will, as a rule, leak enough to be detectable by chemical test. Before the test is carried out the patient must be put on a special diet containing no meat, fish, fowl, or green vegetable, or anything prepared from them. As a derivative of hæmoglobin is being tested for, it must not, of course, be ingested; chlorophyll is chemically indistinguishable from hæmoglobin, and for that reason it also must be excluded.

Inquiry must also be made for bleeding gums, etc., and it is advisable that the teeth should not be brushed during the period of the test, so that there may arise no fallacy from that source.

About four days should be allowed to transpire from the commencement of the diet before the first specimen is obtained; specimens should then be examined on three or four successive days, the patient meantime remaining on the diet. The material selected should be formed, and a piece for the test taken from the centre of the mass. In this way any blood derived from low down the intestinal tract may be excluded.

In my experience the benzidin test, carried out in test tubes with reliable reagents and proper precautions, is the best for ordinary routine work.

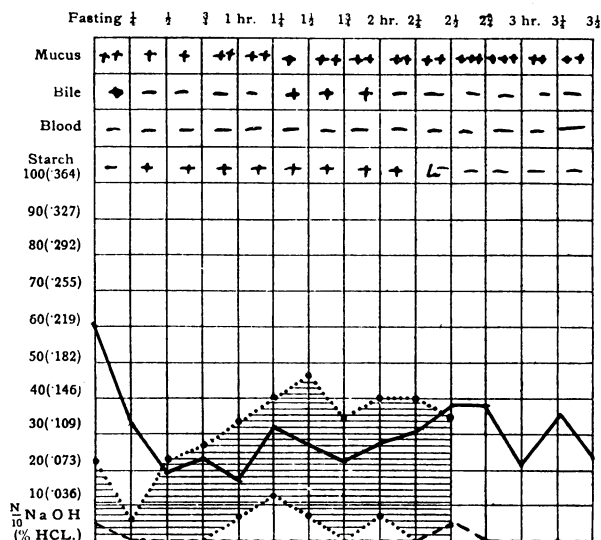
1. GASTRITIS.

The fractional test meal picture varies with the length of time during which the disease has been present. In the very early stages the resting juice, which normally lies between nothing and one hundred cubic centimetres in volume, may be increased and have a raised content of free hydrochloric acid. This increase of free acid may be demonstrable throughout the meal.

It is more often when the trouble has been existent for some time that a gastric analysis is undertaken. The resting juice will then be likely to be small in amount and may consist almost entirely of thick mucus, containing a considerably increased number of polymorphonuclear cells. Hypo-acidity is almost constant and, together with the large increase of mucus, is found throughout the test. Anacidity is present in about fifty per cent. of cases. Combined acid is usually increased, probably as a result of the partial combination of hydrochloric acid with mucus. In this way the hypo-acidity is also in part explainable, but, in addition, the mucus by its physical action decreases the activity of the secreting cells. It is well known that lavage of the stomach, if carried out for a period, will almost invariably cause a rise in hypo-acid curves and produce free acid in many stomachs where anacidity has previously been demonstrated. In gastritis, occult blood is occasionally found on testing the fæces, but as a rule only a faint reaction is obtained, and it is rarely persistent through a series of consecutive specimens.

2. GASTRIC ULCER.

Fractional test meal findings show great variation and are often of little assistance. A great deal depends on the position of the ulcer. Those high up on the lesser curvature may give a fractional test meal normal in every respect or, perhaps, showing some hypo-acidity. On the other hand, if the site be close to the pylorus, hyperacidity is very much the rule, and a curve similar to that which is so typical of duodenal ulcer will often be obtained. Proximity of the ulcer to the pylorus seems to be the determining factor in the production of this type of curve.



2. CURVE FROM A CASE OF GASTRITIS.

Free hydrochloric acid is practically absent. Combined acidity is high. There is a large amount of mucus present in all specimens.

The lowering of the free acid curve in some cases of gastric ulcer is probably caused by the gastritis which is a constant accompaniment. The presence of excess mucus points to this, and lavage has been found to bring about a rise to normal or even a hyperchlorhydria, dispelling the mucus at the same time. Occult blood tests are generally positive when the ulcer is active, as may be judged by pain and discomfort. One may often safely secure activity in a quiescent case, for the purpose of the test, by getting the patient to eat food and do things which are known to produce symptoms.

3. CARCINOMA OF THE STOMACH.

The fractional meal findings depend on (a) the type of the lesion, (b) whether it is producing obstruction, and (c) whether it presents an ulcerating surface in the gut cavity.

(a) Many sufferers from gastric carcinoma are found to have achlorhydria, and this is especially likely in the diffuse "leather-bottle" type.

(b) Obstruction is generally accompanied by a marked increase in the combined acid, and when the obstruction is of high degree the findings are generally characteristic. The resting contents are then often large in amount and foul-smelling, contain charcoal and food ingested twelve or more hours previously, shreds of tissue, and, sometimes, blood. There is little or no free hydrochloric acid and no bile. During the meal there is generally achlorhydria with high combined acid, persistent starch, and no bile. At the end of three hours the greater portion of the meal will be aspirated from the stomach.

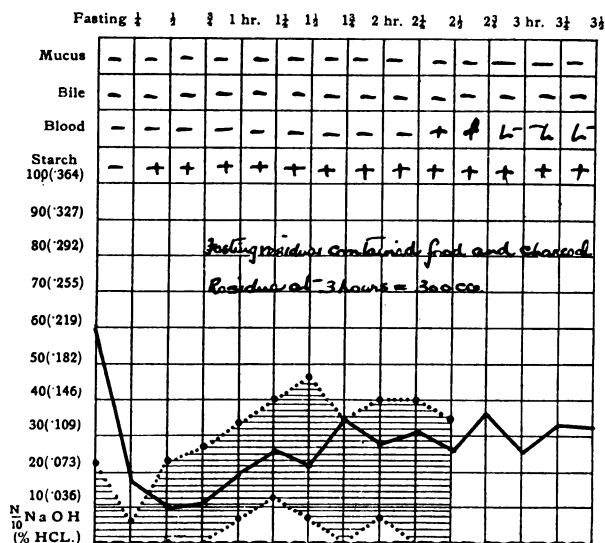
Obstruction caused by cicatrization of an ulcer does not, as a rule, give the same foul mess, and the combined acidity is not so high.

(c) When there is ulceration of the growth, an alkaline fluid exudes from the raw surface, and it is the combination of this with gastric juice which probably produces the high combined acidity. There is also constantly some bleeding, greater or less in amount, often giving rise to the presence of gross blood in the specimens and positive occult blood reactions on testing the stools.

4. DUODENAL ULCER.

It is in duodenal ulceration that gastric analysis is most frequently helpful in ordinary everyday clinical work. Duodenal ulcer is a comparatively common condition—much more common than gastric ulcer, for example, among cases which are seen by the consulting physician. This is surprising, for at autopsy scars of chronic ulcers in stomach and duodenum seem to be found with almost equal regularity. It is possible that either gastric ulcers are more frequently healed by simple measures or that they give rise, on the average, to less pain and inconvenience and are tolerated with less complaint.

The typical curve found in duodenal ulceration without obstruction presents the following characters. The resting juice is very variable in amount, being sometimes up to 100 c.cs. or more: it is usually perfectly clear, without mucus, and highly acid. Dilution with the gruel produces a fall of the acid to, or approaching



3. CURVE FROM A CASE OF PYLORIC OBSTRUCTION CAUSED BY CANCER.

No free hydrochloric acid. Combined acid is high. The character of the fasting residue and the large amount remaining at the end of three hours are of importance. Blood was present in the later specimens and starch throughout the test. No bile was present.

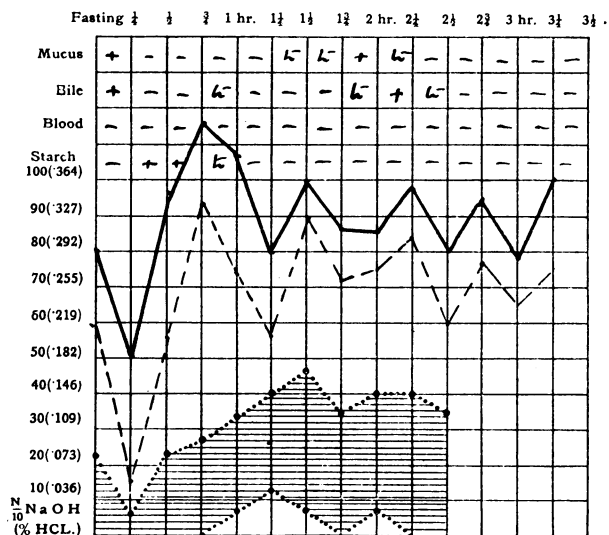
nothing, but thereafter there is a steady rise to a high figure, often 70 or 80 and sometimes exceeding 100 c.cs. Emptying, which is indicated by the disappearance of starch, is, as a rule, rapid, being often complete in an hour or little more. In spite of this there is often no fall in acidity, indicating the failure of regurgitation from the duodenum, and continued after-secretion produces a sustained high plateau which may go on indefinitely if no further food be ingested. It is important in all fractional test meals to try to obtain specimens over the full period of three hours. This is especially so when duodenal ulceration is suspected, otherwise the high acid plateau of secretion after the stomach has emptied may be missed. It is the continued hypersecretion of this highly acid juice, together with the hyperperistaltic stomach and spastic pylorus almost always associated with it, which prevent regurgitation of the alkaline duodenal contents, and so determine the high continued acidity in the stomach. For the same reason, bile is rarely present in many of the specimens or to any great amount.

Where a considerable degree of obstruction is present the picture will necessarily be modified. The resting juice will be large in amount, depending on the degree of obstruction, and may contain some of the charcoal swallowed twelve hours previously. Partially digested food may even be present. Owing to the volume of the stomach contents, and also to the gastritis which the retention gives rise to, the acid curve will not be so high. Bile is likely to be completely absent, and a large portion of the meal will be aspirated when the stomach is emptied at the end

of three hours. The bulk may, indeed, be in excess of the pint of gruel swallowed, owing to hypersecretion of gastric juice.

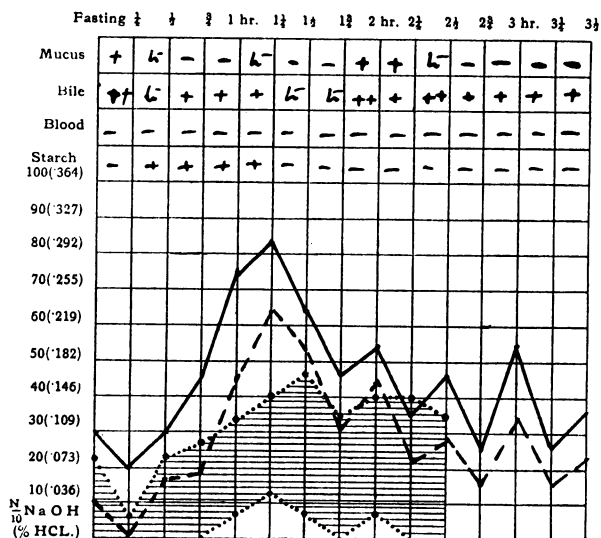
Occult blood tests can be of great help where duodenal ulcer is suspected. Disease in other organs may give rise to symptoms very similar to those produced by it—chronic appendicitis, abdominal adenitis, chronic cholecystitis, for example—and often there seems to occur a condition which, in the absence of very definite knowledge, we refer to as “duodenitis,” which is almost indistinguishable clinically. This last may give very suggestive radiographic appearances, and the fractional meal is often typical of duodenal ulcer, as the same pylorospasm and hypertonic stomach often accompany it. In these cases it is of great importance to find the stools giving a series of absolutely negative reactions when tested for blood, especially if the specimens have been obtained during a period when symptoms were active. The presence of constantly strongly positive tests, on the other hand, renders ulcer very likely to be the correct diagnosis.

The test meal findings in duodenal ulcer often give help in choosing cases for the operation of gastro-jejunostomy. It has been found that the cases which give the best results are those showing slower emptying and absence of hypertonus, as indicated by a not excessively high acid curve. On the other hand, the stomach which empties in about an hour, and continues to pour out a highly acid secretion, is unlikely to do well. Emptying is likely to be even more rapid and the acid curve may become even higher after the operation than it was before. Little or no relief of symptoms will result, and conditions are ideal for the production of an ulcer at the junction. Gastro-enterostomy was originally performed only for the relief of



4. CURVE FROM A CASE OF DUODENAL ULCER WITH EXTREME HURRY.

Stomach is empty in three-quarters of an hour. Free hydrochloric acid is very high, and remains so after the stomach is empty.

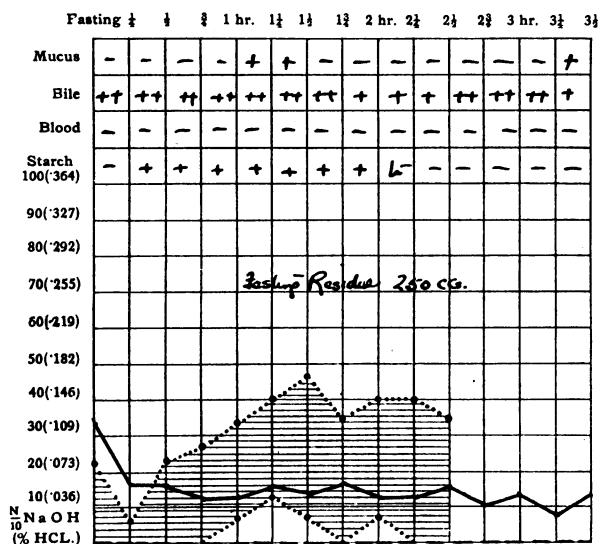


6. CURVE FROM SAME CASE AS FIG. 5, FOLLOWING GASTRO-ENTEROSTOMY.

There is a good regurgitation of duodenal contents, reducing the hyperchlorhydria both in degree and duration. The period of emptying is shortened from two and a quarter to one and a quarter hours. Bile is present throughout the test.

In normal people, when there is a normal secretion of hydrochloric acid, the contents of the duodenum are generally found to be sterile, but in its absence bacillus coli and enterococci can easily be cultured. It might be expected that these organisms would find their way back into the bile ducts and gall-bladder and, if the local resistance happened to be lowered in any way, set up a cholangitis or cholecystitis.

Duodenal Intubation.—Further information as to the presence or absence of pathological conditions in the gall-bladder may sometimes be obtained by duodenal intubation. By this means bile may be obtained for examination as it is discharged from the common bile duct. When the tube has passed into the duodenum, and reached the vicinity of the ampulla of Vater, amber-coloured bile is first syphoned off. Some solution such as saturated magnesium sulphate in water, which, when it comes in contact with the ampulla or duodenal mucosa will cause a contraction of the gall-bladder, is then injected, and as much of it as possible withdrawn again. This is succeeded by more light amber bile, probably from the common duct, to be followed in turn by dark viscid bile which comes from the gall-bladder. Of this last, careful examination should be made as to the presence and nature of deposit and micro-organisms. Frank pus or even any appreciable number of bile-stained leucocytes indicate an active inflammatory process. In the early catarrhal stage there will often be found numbers of high columnar epithelial cells deeply stained by bile and of gall-bladder origin. The presence of crystals of cholesterol, calcium or bilirubin, or of a large amount of bile-stained epithelial debris, is strongly suggestive of



7. CURVE FROM A CASE OF "VICIOUS CIRCLE" VOMITING FOLLOWING GASTRO-ENTEROSTOMY.

Free hydrochloric acid is absent. Bile is present in very large amounts throughout the test. In spite of the normal emptying time, there was a large amount of fluid present in the stomach at the beginning of the meal.

calculus formation. The importance of the epithelium, etc., being bile-stained, is that it indicates the origin of the material to be in the biliary tract, while that coming from the stomach, duodenum, or pancreas is not so discoloured.

I do not think we are on such safe ground when we come to deal with bacteriological examinations. The method by which the test must be carried out is anything but aseptic. In the mouth and pharynx the tube must be grossly infected during swallowing, and although various methods of preventing this, such as that of filling up the orifices in the bulb with paraffin wax and expelling it by air pressure when the tube has entered the duodenum, have been tried, they have not produced much improvement. When achlorhydria is present, I do not think any great reliance can be placed on cultural findings alone, and only the presence of gross infection, as demonstrated by examination of stained direct preparations, and proof by subsequent culture that the organisms are viable, can be taken as evidence of bacterial pathology. In material obtained by duodenal intubation one frequently finds a gram positive diplococcus, in appearance similar to the pneumococcus, present in large numbers, but which does not grow on culture under ordinary conditions. It is probably a pneumococcus derived from the mouth and pharynx which has been rendered non-viable, either by hydrochloric acid in passage through the stomach or by bile in the duodenum.

When hydrochloric acid is present in the stomach, one ordinarily obtains specimens from the duodenum which are not grossly contaminated, and the finding

of any viable organism in fair numbers, either on direct examination or culture of the bile on a solid medium, is very suggestive of a definite gall-bladder infection.

Just as the failure to find tubercle bacilli in a slide prepared from a sample of sputum does not exclude this infection, so negative findings from a duodenal intubation do not exclude disease of the gall-bladder; the examination merely provides one point which may help in coming to a conclusion when the whole picture is considered.

Van den Bergh Reaction.—The Van den Bergh reaction has not proved of so much practical help in the diagnosis of biliary obstruction as had at first been hoped. When an increase of bilirubin in the blood is caused by obstruction to the flow of bile, with reabsorption, it gives what is known as a “direct” Van den Bergh reaction: when it is due to an increased production of bile, as in certain blood diseases, it gives an “indirect” reaction: when damage to liver cells is the causation it gives a “biphasic” reaction. In this way it would appear easy to determine the cause of jaundice in any particular case, but, unfortunately, when obstructive jaundice has been present for more than a day or two, a secondary hepatitis supervenes, the liver cells themselves becoming deranged and giving rise to a further increase in bilirubinæmia. The biphasic reaction thus produced masks any direct reaction present, so that it is only in the first day or two that an obstructive jaundice can be distinguished from one of liver origin. That it should be so is unfortunate, as the determination of the origin of a jaundice as to whether it is primarily obstructive or hepatic is one which has frequently to be made and is often of the greatest importance. The test is of great service, however, in deciding whether there is any increase of bilirubinæmia, and, if so, whether it is of hæmatogenous origin in contra-distinction to biliary.

7. APPENDICITIS AND ABDOMINAL ADENITIS.

Acute appendicitis is frequently diagnosable with the greatest certainty, but in atypical cases doubt sometimes arises. This seems to be especially so when the stage of abscess formation may have been reached, and it is then that a leucocytic count may be of service. When the white-cell count of the blood rises to 15,000 per cubic millimetre, with a high percentage of polymorphonuclears, it is probable that pus is present, and when it reaches 20,000 it is pretty certain to be. Unfortunately, pus does not always produce a considerable leucocytosis, so that it is only the positive finding which is of value.

In chronic appendicitis and abdominal adenitis, the fractional test meal results are very variable. When the symptoms are suggestive of duodenal ulceration, there is often obtained a curve which also might denote this condition, though marked hyperchlorhydria with rapid emptying is uncommon. More frequently the curve will be of the type slowly mounting to a moderate height, with starch still present in the stomach at three hours. In appendicitis, occult blood tests are generally negative, though in adenitis they are often positive, possibly because of an associated congestion of the mucous membrane. Abdominal adenitis is a most difficult

condition to diagnose clinically with any feeling of assurance. It most often simulates appendicitis or duodenal ulcer. X-ray examinations and laboratory tests are rarely of much assistance, but the obtaining of a well-marked tuberculin reaction in the absence of signs of any other tuberculous infection lends weight to a clinical diagnosis.

8 PANCREATITIS AND PANCREATIC TUMOURS.

In acute pancreatitis the pathologist is often able to clinch a diagnosis already suspected, and so avoid a laparotomy which may easily be disastrous. The urinary excretion of diastase is in normal health remarkably constant, lying between ten and twenty units. In acute pancreatitis it practically invariably shows a considerable increase, and may rise up to two or three hundred units. As the test takes only about three-quarters of an hour to carry out, it is of great practical assistance.

Some alteration in the urinary diastatic content may be found in chronic pancreatitis, it being sometimes more, sometimes less. Frequently, however, the figure obtained is within normal limits.

Chronic pancreatitis and neoplasm generally show themselves by a failure of digestive secretion, and if the stool be examined while the patient is on an ordinary mixed diet it will be found to contain pathological amounts of starch, undigested muscle-fibre, and fats. The muscle can be seen by direct microscopic examination, as can also the starch after staining with iodine. By various dyes the fats can often be shown up also if there is a total increase, but it is better to do an exact quantitative analysis, determining total fat, unsaponified fat, neutral fat, and free and combined fatty acids. The total fat is often trebled, and a large proportion of the increase will be found in the neutral fats, owing to defective fat splitting. In obstructive jaundice the total may be equally increased, but, since the fat-splitting action is normal, the increase is in the fatty acid fraction.

9. DISEASES OF THE LARGE INTESTINE.

In the large intestine the only two conditions in which the laboratory is directly helpful in diagnosis are malignant disease and acute diverticulitis — malignant disease only when there is ulceration into the lumen of the gut and when an occult blood reaction is obtained, and acute diverticulitis when inflammation of a diverticulum has produced pus and a polymorphonuclear leucocytosis is likely to be found.

This brings us to the end of the important pathological conditions of the digestive organs in the elucidation of which the clinical pathologist can assist. Laboratory tests can be of considerable help so long as it is realized that, for the most part, they are not of themselves diagnostic, but, like other methods of examination, simply provide points of evidence by the co-ordination and assessment of which a diagnosis may be made.